PATENT COOPERATION TREATY

23 FEB 2005

1525384

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 31422P WO	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP 03/09398	International filing date *(day/month/year)* 25.08.2003	Priority date *(day/month/year)* 23.08.2002
International Patent Classification (IPC) or both national classification and IPC A61K9/127		
Applicant MUNICH BIOTECH AG et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
27.01.2004	03.11.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Greif, G Telephone No. +49 89 2399-8659

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/09398

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-37 as originally filed

Claims, Numbers

1-22 as originally filed

Drawings, Sheets

1/6-6/6 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 21 (in part)

   because:

   ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

   ☒ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. 21 (in part) are so unclear that no meaningful opinion could be formed *(specify)*:

   see separate sheet

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	5-16,19,20,22
	No:	Claims	1-4,17,18,21
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-22
Industrial applicability (IA)	Yes:	Claims	1-22
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claim 21 does not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The claim attempts to define the subject-matter in terms of the result to be achieved which merely amounts to a statement of the underlying problem. The technical features necessary for achieving this result, i.e. the method steps of claim 22, should be incorporated in claim 21.

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents:

   D1: WO 01/93836
   D2: US 2001/0038851
   D3: US 2002/0065329
   D4: US 6,090,955

2. Novelty

   D1 discloses micelles (a non-vesicular preparation) made of cationic amphiphiles, and additionally other amphiphiles, which also comprise drugs such as camptothecin or platinum complexes, and which can be converted into liposomes (p.9, line 10 to p. 10, line 11; p. 12, lines 19-.26; p. 16, line 19 - p. 17, line 9; p. 18, lines 6-28; p 22, line 24- p. 23, line 9; p, 29, lines 10-31; Table I, p. 31, line 29 - p. 32, line 16; p.43, line 22 - p. 47, line 27; p. 49, lines 4-24; p. 52, lines 10-11; claims 1, 2, 10, 26-28, 31, 40-42). Since all the necessary components as described in claims 1-15 (except for the concentration of cationic amphiphile) are present, and since the liposomes of D1 are of the size of 80 - 160 nm, D1 anticipates the subject-matter of claim 17.
   D2 discloses liposomes comprising cationic amphiphiles lipe DOTAP etc and as entrapped agents platinium compounds, vinca alcaloids or camptothecin

derivatives etc, where the liposome size is about 100 nm ([0055] - [0056], [0072]-[0073], Table 2). Claim 17 lacks novelty over D2; since the liposomes disclosed therein appear to have the same characteristics as the ones claimed in claim 17.
D3 discloses a hydrogel formed by a cationic amphiphile dissolved in water at a concentration of 5-50 mM, whereby an anionic compound is also present (0007, 0008, 0013-0024, 0028, Table I). Claims 1-4, 18 and 21 lack novelty over D3.

3. Inventive Step

In case the applicant would obviate the above novelty-objection, the content of D1 should be considered. It differs from the subject-matter of claims 1-15 in that the concentration range of the cationic amphiphile used to form the micellar preparation is not disclosed. However, the expert in the field is familiar with determining the CMC of lipids and would therefore be able, without the use of inventive skill, to prepare the preparation of claims 1-15, based on D1. Inventive step can therefore not be acknowledged for claims 1-15.
For the same reason, claims 16-21 lack inventive step over D1.
Claim 22 lacks inventive step with respect to the combination of D1 with D4, said document disclosing preparations of liposomes comprising amphiphiles and taxol by high-pressure homogenisation (column 3, lines 7-37, example 1).